

Appl. No. 09/873,952
Amdt. Dated September 26, 2003
Reply to Final Office Action of March 26, 2003

AMENDMENTS TO THE SPECIFICATION:

Please replace the paragraph beginning at page 4, line 6 with the following amended paragraph:

B1
The essential feature of the invention is a composition which contains an ~~antineoplastic~~ antineoplastic alkylphospholipid, and an antineoplastic antiestrogen in a lipid vesicle. A suitable example of these ingredients is octadecyl-(N,N-dimethylpiperidin-4-yl)-phosphate (OPP), hexadecylphosphocholine, erucylphosphocholine, octadecylphosphoethanolamine, and hexadecylphosphoserine.

Please replace the paragraph beginning at page 5, line 7 with the following amended paragraph:

The alkylphospholipids of the present composition suitably has the formula



wherein

B2
R is a C₁₂₋₂₂ alkyl, alkenyl or ~~alkinyl~~ alkynyl residue;

Y is oxygen, sulfur or a CH₂ residue;

P is a phosphate group (PO₂); and

X is a choline, modified choline residue or serine, ethanolamine, glycerine group, or a synthetic modification of the foregoing groups.

Please replace the paragraph beginning at page 6, line 5 with the following amended paragraph:

B3
A water or lipid-soluble antiestrogen associated with the phospholipid analogs of Formula (I) is suitably tamoxifen, droloxifene, toremifene, idoxifene, raloxifene, ~~miproxifene-phosphate~~ miproxifene-phosphate (TAT-59), ICI 1643,384 ICI 164,384, ICI 182,780 and the main metabolites of tamoxifen, namely 4-hydroxytamoxifen and N-desmethyl-tamoxifen.

Please replace the paragraph beginning at page 6, line 15 with the following amended paragraph:

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B4

Suitably polyethylene glycol modified phosphatidylethanolamine in the molecular weight range of 1000 - 6000 Dalton is used as a PEG lipid. For example, suitable compounds include 1,2-Distearoyl-s,n-glycero-3-phosphoethanolamine-N-polyethyleneglycol, MG2700; (PEG₂₀₀₀DSPE)-1,2-Distearoyl-s,n-glycero-3-phosphoethanolamine-N-polyethyleneglycol, MG2700 (PEG₂₀₀₀DSPE); and 1,2-Dipalmitoyl-s,n-glycero-3-phosphoethanolamine-N-polyethyleneglycol 1,2-Dipalmitoyl-s,n-glycero-3-phosphoethanolamine-N-polyethyleneglycol, MG5750 (PEG₅₀₀₀DPPE). Compounds which are simultaneously a PEG lipid and an anti-neoplastically effective phospholipid analog, are also useful, such as hexadecylphosphoethanolamine-N-polyethyleneglycol.

Please replace the paragraph beginning at page 10, line 8 with the following amended paragraph:

B5

36 mg OPP, 72 mg tamoxifen citrate (Tam), 144 mg phosphatidylcholine (PC) and 8.5 mg DCP and 9.7 mg N (~~O-methyl-polyethyleneglycol~~) 1,2-distearoyl-s,n-glycero-3-phosphoethanolamine-1,2-Distearoyl-s,n-glycero-3-phosphoethanolamine-N-polyethyleneglycol (PEG₂₀₀₀DSPE) are completely dissolved in 100 ml chloroform/methanol (7/3; v/v) and the solvent then completely evaporated on a rotation evaporator. The resulting finely distributed lipid film is resuspended with 12 ml of citric acid/phosphate buffer (pH 6.08) and intensively moved for at least 3 hours at room temperature on a vibration machine following addition of some glass pearls. An MLV suspension is obtained, which is heterogeneous in its size distribution has vesicle diameters of between 100 and 5000 nm. These Tam liposomes are most suitably used for *in vitro* tests and as initial liposomes for vesicles of a defined composition.

Please replace the sentence beginning at page 14, line 13 with the following amended sentence:

B6

The asterisk * means that the result is significantly different from HO-TAM; and a plus sign + means that the ~~result is significantly~~ result is significantly different from MCF7(R-).